REMARKS

By the foregoing amendment, claims 1, 2 and 6 have been amended. Claims 9-30 stand withdrawn from consideration. Claims 31-38 have been added. Claims 1-8 and 31-38 are pending.

Applicants submit that the amendment to the claims is supported in the application as originally filed as follows:

Claims 1-8 originally recited both DNA encoding a polypeptide (see subpart (a) of original claim 1) and DNA that hybridizes DNA encoding a polypeptide (see subpart (b) of original claim 1). Claims 1-8 have been limited to DNA encoding a polypeptide, i.e. original subpart (a). Original subpart (b) has been moved to newly presented claims 31-38. Accordingly, support for amended claims 1-8 and newly presented claims 31-38 is found in the originally filed claims, as well as throughout the specification. Claim 33 recites antisense and probe DNAs. Antisense DNA is particularly taught at page 50, lines 3-17 of the specification. Probes are taught at e.g. page 45, lines 15-26 of the specification. No new matter has been added by the foregoing amendment.

I. Response to Restriction Requirement

Applicants acknowledge that the requirement for restriction has been made final. Applicants further acknowledge that they have elected Group I, claims 1-8, without prejudice, and that claims 9-30 have been withdrawn from consideration. Applicants request that claims 9-30 be held in abeyance until allowable subject matter is identified in the present application.

Applicants further acknowledge the subgroup restriction to Subgroup VIII, SEQ ID 97. While Applicants disagree with the Office Action's assertion that a search of all the recited Subgroups would be unduly burdensome, in order to expedite prosecution. Applicants have amended claims 1, 2 and 6 to limit the claims to Subgroup VIII. This amendment is made without prejudice to pursuing the non-elected Subgroups in one or more copending applications.

II. Priority

The Office Action presents an objection to the priority paragraph at the beginning of the specification. By the foregoing amendment, the first paragraph of the specification has been

replaced with an amended paragraph, including the provisional serial numbers that were unavailable at the time that the instant application was filed. Applicants submit that this amendment is sufficient to overcome the Office Action's objection.

III. Claim Objections

The Office Action presents an objection to claims 2 and 6 under 37 CFR § 1.75(c), on the basis that claim 6 was improperly dependent upon claim 2. By the foregoing amendment, claim 6 has been amended to appear in independent form, thereby obviating the objection to claims 2 and 6. Applicants accordingly request withdrawal of this objection.

IV. Utility

The Office Action rejects claims 1-8 under 35 USC § 101 for lack of a patentable utility. Applicants traverse this rejection for the following reasons.

As best understood by the undersigned, the Office Action accepts the utility of the claimed nucleotide of SEQ ID NO: 96 as being credible (Office Action page 6), but finds that the utility is not well-established, specific and substantial. Also, as best understood by Applicants, the credibility the utility of a DNA encoding a polypeptide of SEQ ID NO: 97 has not been challenged. Nor has the credibility of the utility of a DNA that hybridizes to a DNA encoding a polypeptide of SEQ ID NO: 97 been challenged. As best understood by the undersigned, only the specificity and substantiality of the claimed nucleic acids have been challenged. Applicants submit that there is ample teaching of substantial and specific credible utility for the claimed nucleic acids, and that the Office Action therefore fails to establish *prima facie* lack of utility.

As stated in the most recent edition of the Utility Guidelines, in order for the Patent Office to establish that a claim lacks utility, it must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. 66 Fed. Reg. 1092, 1098 (2001). The *prima facie* showing must contain the following elements: (1) a clear explanation of why the claimed invention is not specific and substantial or well-established, (2) support for factual findings relied upon for (1), (3) an evaluation of all evidence of record. Id. A rejection based on lack of utility should not be

maintained if an asserted utility for the claimed invention would be considered specific, substantial and credible by a person of ordinary skill in the art in view of all evidence of record. Id. Assertions of fact in the specification must be accepted as true unless adequately rebutted by evidence. 66 Fed. Reg. 1092, 1098-1099. Applicants submit that each of the rejected claims possesses at least one asserted utility that is substantial, specific and credible.

The specification discloses that CLAN-A, can trigger pro-caspase-1 activation by the "induced proximity" mechanism. See application page 16, lines 24-28. There is no reason given in the Office Action to doubt the objective validity of this statement. In turn, pro-caspase-1 activation is implicated in apoptosis. Caspases are the principal effectors of apoptosis. Specification, page 3, line 6. Thus, one of skill in the art would thus understand that CLAN-A can, by activating pro-caspase-1, effect apoptosis. It is well-known in the art that apoptosis, or programmed cell death, is important for tissue homeostasis, for eliminating infectious agents and for treatment of cancer. See specification, pages 86-87. In addition to inducing apoptosis in cell systems, CLAN-A-encoding nucleotides can be used to develop probes, to detect the presence of CLAN-A in tissues and cell lines. See for example specification, page 120 (disclosing northern-blot analysis demonstrating lung- and spleen-specific expression of CLAN-A), page 121 (disclosing RT-PCR using claimed primers), and page 122 (detecting CLAN expression in cell lines). CLAN-A-encoding nucleotides can also be used to prepare antibodies to CLAN-A; CLAN-A can be expressed in transformed cell-lines, then isolated and used to prepare antibodies. See for example page 127 (describing anti-CLAN-A antibodies in conjunction with anti-epitope antibodies. The Office Action does not give any reason to doubt the objective truthfulness of any of these assertions. As the Patent Office must accept assertions made by Applicants in their specifications, Applicants submit that a substantial and specific, credible utility has been established for CLAN-A.

Claims 1-8 embrace, in addition to SEQ ID NO: 96, other DNA that encodes a polypeptide of SEQ ID NO: 97, DNA that hybridizes under moderately stringent conditions to said DNA, or a nucleotide of at least 15 contiguous bases of one of the aforementioned DNAs. Applicants submit that there is sufficient, specific and credible utility for each of these nucleic acids in the specification.

There is sufficient substantial and credible utility disclosed in the specification for DNA that encodes a polypeptide of SEQ ID NO: 97. As Applicants have argued above, CLAN-A possesses substantial specific and credible utility. Applicants submit that, due to the degeneracy of the genetic code, DNA that encodes a polypeptide of SEQ ID NO: 97 possesses patentable utility, as there is no reason to doubt that the person having skill in the art would recognize that a DNA differing from SEQ ID NO:96, but encoding SEQ ID NO: 97, would be capable of being expressed *in vitro* or *in vivo* via a suitable expression vector system. Thus, as CLAN-A possesses sufficient specific and credible utility within the meaning of § 101, so also does a DNA encoding CLAN-A.

There is also sufficient substantial and credible utility disclosed in the specification for DNA that hybridizes to a DNA encoding a polypeptide of SEQ ID NO: 97. The specification discloses, for instance, that DNA that hybridizes to a DNA encoding CLAN-A can be used to detect the presence of such CLAN-A encoding DNA in an assay. See specification, page 49. Since there is no objective reason given to doubt that this specific utility is substantial and credible, Applicants submit that a DNA that hybridizes CLAN-A encoding DNA possesses sufficient specific and credible utility within the meaning of § 101.

There is also substantial specific and credible utility for a shorter DNA of at least 15 contiguous nucleotides of a DNA encoding, or hybridizing to DNA that encodes, CLAN-A. The specification teaches that such shorter DNA segments can be used to detect CLAN-A encoding nucleic acid, such as mRNA. See specification, page 48. Such shorter DNA can also be used as an antisense nucleic acid. Specification, page 50. Since there is no objective reason given to doubt the utility of such shorter DNA segments, Applicants submit that they too possess substantial specific and credible utility within the meaning of § 101.

The undersigned understands the Office Action to hold that the utilities given for CLAN-A in the specification are not substantial enough to meet the utility requirement of § 101. As best understood by the undersigned, the Office Action requires that CLAN-A have utility as a therapeutic in order for CLAN-A to have a practical, "real world" utility worthy of patenting. Applicants submit that utility as a therapeutic is not necessary for patenting of either a nucleic acid. Thus, the citation of Damiano et al. at page 7 of the Office Action is irrelevant to

patentability of the claimed nucleic acid. The question is not whether the nucleotide possesses therapeutic effect, but whether the person having skill in the art would recognize that the nucleotide possesses substantial specific and credible utility. As stated above, the specification contains teaching of substantial specific and credible utility for each of the claimed nucleic acids, and there is no objective reason given why any of these teaching would be doubted by the person having skill in the art.

Applicants disagree with the assertion that Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1996) supports the § 101 rejection. In Manson, the Supreme Court considered a case where there was no stated utility for the claimed compound within the four corners of the patent. 383 U.S. at 521, 148 USPQ at 690. The only utility asserted was one raised *ex post* by the applicant's attorney, based on the theory that, since the claimed compound was structurally similar to other steroids that possessed therapeutic effects, the claimed compound also possessed similar utility. 383 U.S. at 522, 148 USPQ at 690. In contrast, the present specification is replete with disclosure of practical utility. Nucleic acids according to the invention can be used to make CLAN-A, to detect the presence of nucleic acids that encode CLAN-A, or as antisense molecules for inhibiting expression of CLAN-A. CLAN-A itself is a CARD-containing compound implicated in apoptosis. As apparently acknowledged on page 6 of the Office Action, the utility of CLAN-A itself is not incredible. There is no objective evidence why the person having skill in the art would find the utility of the claimed DNA to be lacking.

Applicants also disagree with the Office Action's assertion that there is no specific utility asserted for the claimed DNA, which encodes CLAN-A. On the one hand, the Office Action requires that there be a phenotype associated with CLAN-A expression or inhibition, and on the other hand the Office Action discounts the specification's clear teaching that CLAN-A expression is implicated in apoptosis. Indeed, at page 16, lines 24-47, the specification clearly states that CLAN-A can trigger pro-caspase-1 activation. Caspases are the principal effectors of apoptosis. Specification, page 3, line 6. One of skill in the art would thus understand that CLAN-A can, by activating pro-caspase-1, effect apoptosis. It is well-known in the art that apoptosis, or programmed cell death, is important for tissue homeostasis, for eliminating infectious agents and for treatment of cancer. See specification, pages 86-87. The Office Action

does not give any reason to doubt the objective truthfulness of these assertions. Accordingly, a rejection under § 101 is misplaced.

The Office Action concludes with a statement that the example tracks exactly with example 9 of the Utility Guidelines, FR 64(244), December 21, 1999. As an initial matter, Applicants submit that the more recent Utility Guidelines at FR 66(4), pp 1092-1099, January 5, 2001, a copy of which is enclosed herewith, provides the better authority on how the Patent Office is to deal with the utility requirement.

Applicants also submit that, contrary to the Office Action's assertion, the DNA of the present claims do not lack any specific biological effect. On the contrary, as stated above in detail, the specification is replete with teaching of substantial specific and credible utility for the claimed DNA. It is only by ignoring this teaching, which no objective and reasonable person of skill in the art would do, that the Office Action can arrive at the conclusion that the claimed DNA lacks patentable utility. Applicants have taken great pains to characterize the utility of CLAN-A, and to provide specific teaching of how the claimed DNA can be used to express, detect expression of, and inhibit expression of CLAN-A, as discussed in detail above. This is in stark contrast to the situation where a claimed nucleic acid has no stated utility whatsoever. Accordingly, Applicants submit that the position staked out by the Office Action is untenable and the rejection under 35 U.S.C. § 101 should be withdrawn.

V. Enablement

The Office Action rejects claims 1-8 under 35 U.S.C. § 112, first paragraph as lacking enablement. For the reasons set forth below, Applicants submit that the rejection is untenable as applied to the amended claims; withdrawal of the rejection is requested.

As best understood by Applicants, although the Office Action goes to great pains to set out to address each "In re Wands" factor, this rejection is premised on the assertion that the claimed nucleic acids lack patentable utility and that the specification therefore fails to teach one how to use the nucleic acids. Applicants submit that the arguments made with respect to the utility, above, are equally applicable to the question of enablement. In particular, as the claimed

nucleic acids possess patentable utility in accordance with Applicants' arguments above, one of ordinary skill in the art would have known how to use such nucleic acids.

In the interest of fully responding to the particular points raised by the Office Action, Applicants submit the following:

The Office Action avers that the Nature of the Invention is as follows: "Claims 1-8 are drawn to a system and method of screening using SEQ ID NO:97." Applicants respectfully disagree with this characterization of the invention. Claims 1-3 are drawn to nucleic acids encoding a CARD protein; claim 4 to a vector containing said nucleic acids; claim 5 to recombinant cells; claims 6 and 7 to oligonucleotides; claim 8 to a kit for detecting a CARD-encoding nucleic acid; claims 31-33, 36 and 37 to nucleic acids that hybridize to a CARD-encoding nucleic acid; claim 34 a vector; claim 35 recombinant cells and claim 35 a kit for detecting presence of a CARD-encoding nucleic acid. Applicants submit that it is incorrect to lump all the claims together under the rubric of "systems and methods for screening" without taking into account the limitations of each individual claim; each claim should be considered independently on its own merits. Applicants further submit that they have provided adequate teaching of how to make and use the invention of each claim to comply with § 112, first paragraph.

Applicants respectfully point out that the claims have been limited, without prejudice, to the elected nucleic acids encoding a peptide of SEQ ID NO:97 in accordance with the restriction requirement. Applicants further point out that the breadth of the invention must be assessed on a claim-by-claim basis. Applicants respectfully submit that when properly considered on a claim-by-claim basis, the claims are not unreasonably broad, and the specification provides ample teaching of how to make and use the full breadth thereof.

The Office Action criticizes the amount of guidance provided by the specification to the person of ordinary skill in the art to practice the claimed invention. First, Applicants note the requirement to consider each claim on its own merits. Second, Applicants take issue with the Office Action's assertion that no function is provided for nucleic acids encoding SEQ ID NO:97; Applicants particularly object to this characterization with respect to SEQ ID NO:96. While the Office Action correctly quotes from paragraph 0043, it ignores specific teaching of a substantial,

specific and credible utility provided for the CLAN-A-encoding nucleic acid of the present invention. The present specification is replete with disclosure of teaching how to make and use the nucleic acids of the present invention. Nucleic acids (claims 1-3), vectors (claim 4), and recombinant cells (claim 5) can be used to make CLAN-A. Oligonucleotides (claims 6-7, 31-33, 36-37), vectors (claim 34) and kits (claims 8 and 38) comprising oligonucleotides according to the invention can be used to detect the presence of nucleic acids that encode CLAN-A, or as antisense molecules for inhibiting expression of CLAN-A. CLAN-A itself is a CARD-containing compound implicated in apoptosis. As apparently acknowledged on page 6 of the Office Action, the utility of CLAN-A itself is not incredible. There is no objective evidence why the person having skill in the art would not have been able to make and use the claimed invention by following the description provided in the specification.

The Office Action states: "There a NO working examples in which an oligonucleotide encoding SEQ ID NO:97 is used in any assay for detection or diagnosis of any disease or any other related utility." In response, Applicants note that, even presuming *arguendo* that this assertion is correct, there is no requirement for working examples where the teaching of the specification would have provided the person skilled in the art adequate guidance in practicing the claimed invention. The specification provides teaching of assays to detect CARD-encoding nucleic acids in a sample (page 49), antisense nucleic acids (page 50), and antibodies and their uses as detection reagents (pages 59-63). Moreover, the specification does provide working examples commensurate with the scope of what is being claimed. For example the specification provides: preparation of full-length CLAN-A cDNA (page 116), southern blot analysis (page 117, Figs. 1 and 2), detection of tissue specific variation in CLAN-A expression (page 120) and cloning of CARD-A into pcDNA3 with epitope tags (page 127). Applicants thus submit that the assertion that there are no working examples is factually incorrect, or at least misleading, and should be withdrawn.

The Office Action states that the prior art provides no guidance for practicing the claimed invention; and that the Damiano reference (75 Genomics 77-83 (2001)) suggests that there is no real-world utility for the claimed nucleic acids other than for further investigation. While Applicants are not prepared to concede that the teaching of the Damiano reference would lead the person skilled in the art to the conclusion urged by the Office Action, Applicants submit that

whatever Damiano et al. teach, it is irrelevant to the enablement *vel non* of the instant claims. The Office Action implicitly requires that the claimed nucleic acids possess proven therapeutic value in order to be patentable. This requirement is nowhere to be found in the patent laws, rules, case law or the MPEP. In fact, the MPEP clearly states that "when a compound or composition is not limited to a recited use, any enabled use that would reasonably correlate with the entire scope of the claim is sufficient to preclude a rejection for nonenablement...." MPEP § 2164.01(c) (May 2004)(copies attached). Applicants submit that the present claims fit directly within the category of claims not limited to a recited use. As pointed out above, the claimed nucleic acids, vectors and kits have substantial specific and credible utility, *inter alia* in the preparation of reagents for detecting CLAN-2 *in vitro*. The Office Action fails to provide reasons why the specification would have failed to enable the person having skill in the art to practice the claimed invention as disclosed.

Applicants take no issue with the Office Action's assertion that the skill in the art is high.

The Office Action states in part: "The art of biotechnology, as relates to the association of diseases with particular genes, is highly unpredictable. The claimed sequence is currently an orphan gene." The Office Action then argues that, based on this premise, the teaching of Dujon, 12 Genetics 263 (1996), and Rost et al., 318 J. Mol. Biol. 595-608 (2002), would lead one of skill in the art to the conclusion that the art is highly unpredictable. Applicants traverse this conclusion.

As noted above, the claimed invention is not limited to treatment of a particular disease state, nor is the patentable utility of the claimed invention predicated on the potential use of the claimed nucleic acids in therapy. Applicants' representative has pointed to several utilities, supported by adequate description, which support patentability of the claimed invention. See the remarks with respect to utility, above, in general. Moreover, in contradiction to the Office Action's assertion that CLAN-A is an orphan gene, Applicants clearly teach that CLAN-A can trigger pro-caspase-1 activation by the "induced proximity" mechanism as a result of oligomerization mediated by its NB-ARC (NACHT) domain. (Specification page 16). While it may have been the case that, prior to Applicants' invention, the person skilled in the art would not have recognized a utility for the claimed nucleic acids, this is not the case in view of Applicants' detailed disclosure. Likewise, the teaching of Rost et al. does not contradict Applicants' teaching of a specific activity of CLAN-A. When viewed from the vantage of the

person skilled in the art of genetics (vis-à-vis the art of human therapeutics, as urged by the Office Action), the claimed invention is not particularly unpredictable.

The Office Action also avers that "an immense amount of experimentation would be required in order to define whether the protein is associated with any particular disease state." Applicants submit that the properly construed claims are not limited to therapeutics or diagnosis of a particular disease state, and that the person of ordinary skill in the art, being highly skilled as conceded by the Office Action, and armed with the detailed description (including working examples) of the instant specification, would have received more than enough guidance to practice the claimed invention.

The Office Action concludes that, weighing the Wands factors, undue experimentation would have been required to practice the claimed invention. Applicants submit that the Office Action errs first in failing to correctly construe the claims, and that that incorrect construction leads to an incorrect analysis of the enablement question. As discussed in detail above, the claims, when correctly construed, are not limited to therapy or diagnosis of a particular disease state. Being composition claims, they are thus subject to the lower threshold of enablement set forth in MPEP § 2164.01(c): i.e. that to show lack of enablement, the Patent Office must demonstrate that the claims do not have any patentable utility that is enabled by the specification. Given the detailed teaching of utility discussed in detail above, and especially in view of the high level of skill in the art, it is reasonable to conclude that the person having skill in the art would have been able to make and use the claimed nucleic acids, vectors and kits.

In view of the foregoing arguments, Applicants respectfully request that the rejection under 35 USC § 112, first paragraph, be reconsidered and withdrawn.

VI. Description

The Office Action rejects claims 1-8 as lacking written description. For the reasons set forth below, Applicants traverse this rejection.

Claims 1-8 have been amended to comply with the restriction requirement. Accordingly, written description for the claims is as follows:

Claim 1 is drawn to a nucleic acid encoding a protein of SEQ ID NO:97. The specification teaches the entire sequence of SEQ ID NO:96. Taking into account the degeneracy of the genetic code, the person having skill in the art would have been more than able to immediately envision the entirety of the invention of claim 1.

Claim 2 is drawn to the nucleic acid having SEQ ID NO:96. As mentioned above, the specification teaches this entire sequence. Thus, the specification provides adequate description for this invention.

Claims 3 is drawn to the cDNA of SEQ ID NO:96. As mentioned above, the specification teaches this entire sequence. Thus, the specification provides adequate description for this invention.

Claims 4 and 5 are drawn to vectors and recombinant cells containing the nucleic acid of claim 1. Applicants submit that, as the specification provides adequate description of the nucleic acid of claim 1, the person of ordinary skill in the art would have recognized that Applicants possessed the claimed invention that the specification was filed.

Claims 6, 7 and 8 are drawn to oligonucleotides and kits. Applicants submit that, given the disclosed sequence of SEQ ID NO:96, the person of ordinary skill in the art would have been placed in possession of the claimed oligonucleotides.

In view of the foregoing, it is submitted that Claims 1-8 as amended are adequately described by the originally filed specification. Withdrawal of the 35 USC § 112, first paragraph, written description, rejection is therefore requested.

VII. Anticipation

Claims 1-8 were rejected under 35 USC § 102(b) as being anticipated by Adams et al. Applicants respectfully traverse this rejection. Applicants submit that, as amended, the present claims require the presence of at least the nucleic acid encoding a peptide of SEQ ID NO:97, whereas the alignment in Adams et al. makes it clear that the reference teaches only 477 nucleotides (encoding only 159 amino acids) of the claimed nucleic acid sequence. See attached page 59 from the publication corresponding to the instant application (2002/0176853), where for the convenience of the Patent Office, the peptide encoded by the Adams et al. nucleic acid is indicated in brackets. Applicants submit that the teaching of Adams et al. would not have anticipated the claimed nucleic acid encoding a peptide of SEQ ID NO:97. Accordingly, the reference would not have taught SEQ ID NO: 96, vectors, or kits as claimed.

VIII. Conclusion

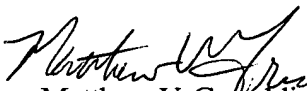
Applicants submit that the foregoing amendments and remarks represent a *bona fide* response to the outstanding Office Action and that claims 1-8 and 31-38 are in condition for allowance. Such action is therefore requested.

If the Primary Examiner finds that allowance may be expedited, Applicants invite him to contact the undersigned directly at the telephone number below.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT WILL & EMERY LLP



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